Final script from "Adult Immunization Update" satellite broadcast, June 26, 2003.

Hepatitis B segment.

Our next topic is Hepatitis B disease, which is caused by the Hepatitis B virus, or HBV. Hepatitis B remains a major public health problem in the United States, even though a safe and effective vaccine has been available for twenty years. Hepatitis B vaccine is also the single most frequent topic of questions we receive.

HBV is the most common cause of chronic viremia known, with an estimated 200 to 300 million chronic carriers worldwide. The virus is an established cause of chronic hepatitis and cirrhosis. HBV is a human carcinogen, estimated to be the cause of up to 80% of hepatocellular carcinomas, or liver cancer. Only tobacco is a more frequent cause of cancer than hepatitis B virus.

A person can die from either an acute or chronic infection with HBV, but most of the mortality results from long term carriage of the virus. Unfortunately, short of a major breakthrough in the treatment of chronic HBV infection, the number of annual deaths will not change very much in the near future. This is because it usually takes 20 years or more of chronic infection to result in end stage liver disease. So even if transmission of hepatitis B virus were completely stopped today, deaths from chronic infection would continue to occur for many years to come.

In the last five years, an average of 9,000 NEW cases of hepatitis B infection have been reported each year. But these REPORTED cases only represent a fraction of the actual incidence. It's estimated that in the pre-vaccine era, 200 to 300 THOUSAND people were infected annually with hepatitis B virus.

Because of vaccination, and risk reduction behaviors in high risk groups, the number of people newly infected in the United States has declined to an estimated 78,000 per year. More than 80% of these new infections are among adults. But there are estimated to be 1.25 million persons chronically infected with HBV in the U.S. An additional 5,000-8,000 persons will become new carriers each year. An estimated 4,000-5,000 deaths from HBV induced liver cancer and cirrhosis occur each year in the United States. HBV is

the third most common cause of death among vaccine preventable diseases in the United States, after influenza and pneumococcal disease.

Risk factors for infection with HBV have not changed very much in the last twenty years. In the 1980s, sexual contact accounted for more than half of cases, and injection drug use accounted for about 15%. This graphic shows the distribution of risk factors in 2001. Persons with multiple sexual contacts, men who have sex with men, and sexual contact with a person known to have HBV infection account for 54% of cases with a known risk factor. Injection drug use accounts for 20% of cases. About 3% of cases are in people who have household contact with a person with acute or chronic hepatitis B. Not surprisingly, the risk of HBV infection increases the longer you are in a risk group. So often, by the time a person is identified as being at risk, they are already infected.

In the early 1980s, health care workers accounted for 2% of HBV infections- 2,000 or 3,000 new infections each year. Since that time, the rate of infection among health care workers has declined by 95%, and is now lower than the rate for the general population. Hepatitis B vaccine has made occupational HBV infection a thing of the past.

The first Hepatitis B vaccine was licensed in 1981. The Hepatitis B surface antigen in the vaccine was derived from the blood of infected people. The two vaccines that are now available in the U.S. came on the market beginning in 1986. They both are composed of recombinant Hepatitis B surface antigen. Vaccine efficacy after a full series of three doses has been estimated at 95%, with a range of 80% to 100%. The duration of immunity is long, 15 years or more. Routine booster doses are not recommended.

Hepatitis B vaccine can and should be administered simultaneously with all other vaccines. For adults it should be administered intramuscularly in the deltoid. No vaccine, including this one, should be administered in the gluteus.

The hepatitis B vaccines available in the U.S. are produced by two different manufacturers- Merck and GlaxoSmithKline. Both companies produce an adult formulation. The adult formulation of Merck’s Recombivax HB contains ten

micrograms per milliliter. Merck also produces a dialysis formulation with forty micrograms per milliliter. The adult formulation of GlaxoSmithKline's Engerix-B, contains twenty micrograms per milliliter. Adults, and by adult we mean anyone 20 years of age or older, should receive one milliliter of Recombivax formulation or the adult formulation of Engerix.

The adult formulation of Engerix has twice as much antigen per dose as Recombivax. But the vaccines are considered to be equivalent and are interchangeable. An adult who begins the series with Recombivax can complete it with Engerix-B, or vice versa. One word of caution- do not be fooled by the higher antigen content of Engerix. The fact that it has twice the antigen per dose does not mean that it is a better vaccine, or that you can give a half dose if you substitute Engerix for Recombivax.

A complete series of Hepatitis B vaccine is three doses. The first 2 doses should be separated by at least one month. The third dose is usually given 4 to 6 months after the second, but the minimum interval is two months if an accelerated schedule is required. The third dose should be separated from the first dose by at least 4 months.

Hepatitis B vaccine is also available in a combination with hepatitis A vaccine, as Twinrix. We discussed the use of this vaccine in the hepatitis A segment of the program.

As with all vaccines used routinely in the U.S., it is NOT necessary to restart the series or add additional doses if the interval between doses is prolonged. Just continue the series where it was interrupted. The reason it's not necessary to restart the series, or to add doses, is because of immunologic memory. This is also the reason that booster doses are not recommended. Persons who respond to the vaccine develop immunologic memory following vaccination. This means that B lymphocytes have developed that are ready to produce more antibody the next time hepatitis B surface antigen is encountered. Antibody may drop to a low level but re-exposure to HBV leads to an anamnestic, or memory response, and the antibody level increases very quickly. Since the incubation period of HBV long- it can be up to 6 months- the immune system can mount a protective response before the virus can do any damage. Asymptomatic HBV infection has been occasionally documented in persons who responded to the vaccine. But chronic

infection rarely occurs among vaccine responders. Since chronic infection leads to severe sequelae, and causes most of the mortality, it is what we most want to prevent.

Booster doses of hepatitis B vaccine are NOT recommended routinely for any group, because there is no evidence that they are necessary for continued protection.

The duration of hepatitis B immunity following vaccination will continue to be studied for many years to come, particularly among those vaccinated as infants. If breakthrough infections, particularly chronic infections, begin to appear ten or 20 or 30 years from now, booster doses may be needed. But not now.

Hepatitis B vaccine is recommended for adults who are at increased risk of HBV infection. Adults who are at increased risk of HBV infection include men who have sex with other men, heterosexuals with multiple sexual partners, persons diagnosed with a recently acquired sexually transmitted disease, and commercial sex workers. Injection drug users who share needles are at extremely high risk for HBV infection. All injection drug users who are susceptible to HBV should be vaccinated as soon as possible after their drug use begins. Male prison inmates are at increased risk of HBV infection because of injection drug use, homosexual activity, or other factors. The prison setting provides an access point for vaccination of inmates with a history of high risk behavior. Persons receiving hemodialysis are at increased risk of HBV infection because of contact with large amounts of blood. Although hepatitis B vaccine is less effective in these patients, it is recommended for all susceptible hemodialysis patients. The risk of health care workers contracting HBV infection depends on how often they are exposed to blood or blood products through percutaneous and mucosal exposures. Any health care or public safety worker may be at risk for HBV exposure, depending on the tasks they perform. If the tasks involve contact with blood or blood-contaminated body fluids, then these workers should be vaccinated.

Other adult candidates for hepatitis B vaccine include: staff and clients in institutions for the developmentally disabled; Alaskan natives, Pacific Islanders, and immigrants and refugees from hepatitis B endemic areas; household members of adoptees and others who come from hepatitis B endemic areas; household members and sexual

partners of HBV carriers; persons with extended travel- 6 months or more- to HBV endemic areas; and, recipients of certain blood products, like hemophiliacs who receive blood clotting factor.

A complete series of three doses of hepatitis B vaccine is highly effective in producing immunity. As a result, post vaccination serologic testing is NOT recommended routinely after vaccination of most adults. Post-vaccination serologic testing IS recommended for adults who are on dialysis, or who are immunodeficient, and for certain health care workers. ACIP recommends that health care workers who have contact with patients or blood and are at ongoing risk for injuries with sharp instruments or needles should be tested for antibody after vaccination. Routine testing is NOT recommended for persons at low risk of exposure, such as public safety workers and health care workers without direct patient contact. Testing for antibody to hepatitis B surface antigen should be done one to two months after the third dose of vaccine.

Hepatitis B vaccine is inactivated, and adverse reactions following vaccination are similar to other inactivated vaccines. Adverse reactions following hepatitis B vaccine are mostly local. Local reactions, such as pain at the injection site are reported in thirteen to twenty nine% of recipients. Mild systemic complaints, such as fatigue or headache are reported in eleven to seventeen% of adults. Temperature of more than 37.7 degrees centigrade - which is very low grade fever - occurs in only about one%. Severe systemic reactions are rare.

There's been a lot of publicity in the last year or two about an association between hepatitis B vaccine and multiple sclerosis. Two recent studies examined this hypothesis. These studies found no association between either onset or relapse of multiple sclerosis. These studies and related material on this topic are available on the National Immunization Program website.

The contraindications and precautions for hepatitis B vaccine are similar to those of other inactivated vaccines. The only contraindication is a severe allergic reaction to a vaccine component or following a prior dose. Moderate or severe acute illness is a precaution. Vaccination should be deferred until the acute illness improves.

We are frequently asked if an allergy to thimerosal is a contraindication to hepatitis B vaccine since the adult formulations do contain thimerosal. Allergy to thimerosal is a contraindication to hepatitis B vaccine only if the allergy is severe. Thimerosal is a mercurial preservative used in some vaccines and medications. Most people who claim to be allergic to thimerosal have had a reaction to an ophthalmic solution, like contact lens cleaner. These reactions are usually local, not anaphylactic. But if the person had an anaphylactic reaction to a product containing thimerosal, you need to be extremely cautious in giving hepatitis B or any other vaccine that contains thimerosal. Depending on the person's risk of hepatitis B virus infection, vaccination could still be considered, but would need to be done by someone capable of managing an acute allergic reaction.

Now before leaving the topic of hepatitis B, we would like to emphasize that THE most effective strategy to increase vaccine coverage is to identify settings where high risk persons can be routinely vaccinated. Efforts are now being made to vaccinate people in clinics that treat sexually transmitted diseases, offer family planning or drug treatment services, and in detention centers.

We asked Dr. Harold Margolis, Director of the CDC Division of Viral Hepatitis to tell you more about these efforts.

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